REMARKS

Claim 1 is amended herein to recite that X' is tobramycin; L is a linker group attached to one or more of the hydroxyl or amine groups of the tobramycin moiety, and is selected from esters, amides, ureas, thioureas, imines, acetals, ethers, phosphates, phosphate esters or diesters, thioesters, oximes and hydrazones; and Y is a pharmacokinetic regulator selected from a hydrophobic moiety or a hydrophilic moiety, wherein the hydrophobic moiety is selected from an optionally substituted straight chain, branched and/or cyclic saturated unsaturated hydrocarbon, and wherein the hydrophilic moiety is selected from oligonucleotides up to 20 nucleotides in length, peptides up to 20 amino acids in length, peptide mimics, carbohydrates, oligosaccharides and derivatives thereof.

In view of the amendment to claim 1, the following amendments are made:

claims 2-6 are canceled;

claims 7-8 are amended to depend from claim 1;

claim 9 is amended to refer to the embodiment wherein the pharmacokinetic regulator Y is a hydrophobic moiety selected from an optionally substituted straight chain, branched and/or cyclic saturated or unsaturated hydrocarbon, claim 10 is canceled and claim 11 is amended to depend from claim 9; and

claim 17 is amended to depend from claim 1 and to refer to the embodiment wherein the pharmacokinetic regulator Y is a hydrophilic moiety.

Claims 20 and 21 are amended by deleting the phrase "and/or prophylactic" and claim 28 is amended to delete the phrase "the prevention and/or". Claim 28 is further amended by

replacing the word "microbial" with "bacterial". In view of the amendment to claim 28 to recite a bacterial infection, claim 29 is canceled and claim 30 is amended to depend from claim 28.

Claims 38-67 and 72 are canceled.

The claims are also amended to correct minor informalities such as by changing the word "A" to "The" at the beginning of the sentence in the dependent claims and correcting the misspelled word "beta-lactam" in claim 24.

Support for the amendments to the claims is found, for example, in the original claims and in the paragraph bridging pages 11-12 of the specification.

No new matter is presented.

Applicants previously elected the species a.-structural formula (I) and species i.-aminoglycoside with traverse, as there is no undue burden in searching the additional species.

Applicants also noted that the Examiner indicated that upon allowance of the elected species, Applicants will be entitled to consideration of additional species.

On page 2 of the Office Action, the Examiner objects to the Abstract because it is not presented in the proper form.

Accordingly, Applicants hereby amend the Abstract as requested by the Examiner.

Additionally, on page 2 of the Office Action, the Examiner objects to Claim 47 because of a typographical error.

Claim 47 is canceled herein, thereby rendering the objection moot.

Moreover, on page 2 of the Office Action, the Examiner rejects Claims 1, 6-32 and 37 and 72 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that while the specification is enabling for tobramycin prodrugs having the structural formula as set forth in Tables 2-4 on page 47-61 of the specification, such does not provide enablement for any aminoglycoside linker group and a pharmacokinetic regulator attached at any position on an aminoglycoside antibiotic.

Claim 1 is amended herein as stated above.

Applicants submit that in view of the specification when read as a whole, one of ordinary skill in the art would be able to practice the invention over the scope claimed without any undue experimentation. The examples provided in the specification demonstrate attachment of various pharmacokinetic regulator groups at different positions around the tobramycin moiety. In this regard Applicants refer the Examiner to the compounds exemplified in Tables 2 and 3 of the specification showing attachment at positions 6", 4", 2", 4', and 6'. These positions represent a primary alcohol or amine that can be reacted in a variety of ways. For example, the 6" OH can be coupled with esters by activation (install leaving group such as 1,2,3-tri-iso-propyl benzene sulfonyl as demonstrated in Intermediate 2) then displacement with a wide variety and number of cesium salts (Intermediates 3). Method A as shown in the specification is used to prepare a variety of compounds in Table 1. The principle of displacement of such an activated leaving group by a nucleophile would be well known to those skilled in the art and a number of nucleophiles could be applied to introduce other linker groups such as thioester, phosphate, hydroxylamine, and hydrazine, and therefore provide access to other compounds, linkers or functional groups as claimed.

Furthermore, the Applicants have shown in the specification as filed that ester linkages can be prepared by the reaction of an OH group with an activated carboxylic acid derivative such as an acid chloride e.g., as used to prepare compounds 25, 29, 31 by Method B. Again, the

reaction of an alcohol with an activated acid is a standard procedure and similar processes could include reaction with a chloroformate to prepare an organic carbonate, reaction with an isocyanate to prepare a carbamate or reaction with an activated phosphate species to form a phosphate diester (e.g., see page 20, no. 3).

It has also been shown that the functionality on the tobramycin moiety can be manipulated to allow other functionality to be incorporated. Examples include activation (e.g., Intermediate 2 as above) or transformation e.g., oxidation to Intermediate 7 (6" aldehyde) followed by reaction with a hydroxylamine to form the oxime ether of Compound 46. It will be appreciated that other reactions are possible with aldehydes, for example reaction with an alcohol or diol to form an acetal, or further oxidation to a carboxylic acid followed by standard coupling with an amine or alcohol to form linkers with different configurations to those prepared from the parent tobramycin alcohols as described above. Amides are prepared by standard coupling methods, e.g., Examples 32 and 33 (Method E).

Accordingly, Applicants respectfully submit that claims are enabled by the present specification, and thus request withdrawal of the Examiner's rejection.

On page 4 of the Office Action, the Examiner rejects Claims 20-21, 28-32, 55-56 and 62-67 under 35 U.S.C. § 112, first paragraph.

Specifically, the Examiner states that while the specification is enabling for the treatment of a bacterial infection, such is not enabling for a method of treatment or prevention of any microbial infection.

Claims 20 and 21 are amended to delete the recitation "and/or prophylactic" and claim 28 is amended by deleting the recitation "the prevention and/or". Claim 28 is further amended by replacing the word "microbial" with "bacterial".

Claim 32 depends from claim 28. Claims 29, 55-56 and 62-67 are canceled.

In view of the amendments to the claims, the Examiner's rejection has been rendered moot.

On page 6 of the Office Action, the Examiner rejects Claims 38-54, 63-67 and 72 under 35 U.S.C. § 103 as being unpatentable over Nakagawa et al, Shecter et al, Umezawa et al or Cron et al.

Further, on page 7 of the Office Action, the Examiner rejects Claims 54-67 and 72 under 35 U.S.C. § 103 as being unpatentable over Nakagawa et al, Shecter et al, Umezawa et al or Cron et al in view of Hendricks et al or Speirs et al.

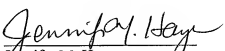
Claims 38-67 and 72 are canceled herein, thereby rendering the rejections moot.

Accordingly, Applicants respectfully request withdrawal of the Examiner's rejections.

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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